



4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2018-D-3292]

Master Protocols: Efficient Clinical Trial Design Strategies to Expedite Development of Oncology Drugs and Biologics; Draft Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a draft guidance for industry entitled “Master Protocols: Efficient Clinical Trial Design Strategies to Expedite Development of Oncology Drugs and Biologics.” This guidance provides advice to sponsors of drugs and biologics for cancer treatment regarding the design and conduct of clinical trials, other than first-in-human (FIH) trials, intended to simultaneously evaluate more than one investigational drug and/or more than one cancer type within the same overall trial structure (master protocols) in adult and pediatric cancers. In contrast to traditional trial designs, where a single drug is tested in a single disease population in one clinical trial, master protocols use a single infrastructure, trial design, and protocol to simultaneously evaluate multiple drugs and/or disease populations in multiple substudies, allowing for efficient and accelerated drug development.

DATES: Submit either electronic or written comments on the draft guidance by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*] to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance.

ADDRESSES: You may submit comments on any guidance at any time as follows:

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: <https://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to <https://www.regulations.gov> will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on <https://www.regulations.gov>.
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

Written/Paper Submissions

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in “Instructions.”

Instructions: All submissions received must include the Docket No. FDA-2018-D-3292 for Master Protocols: Efficient Clinical Trial Design Strategies to Expedite Development of Oncology Drugs and Biologics. Received comments will be placed in the docket and, except for those submitted as “Confidential Submissions,” publicly viewable at <https://www.regulations.gov> or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday.

- Confidential Submissions – To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states “THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.” The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on <https://www.regulations.gov>. Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as “confidential.” Any information marked as “confidential” will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about

FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: <https://www.gpo.gov/fdsys/pkg/FR-2015-09-18/pdf/2015-23389.pdf>.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to <https://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the "Search" box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

You may submit comments on any guidance at any time (see 21 CFR 10.115(g)(5)).

Submit written requests for single copies of the draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10001 New Hampshire Ave., Hillandale Building, 4th Floor, Silver Spring, MD 20993-0002 or the Office of Communication, Outreach, and Development, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 3128, Silver Spring, MD 20993-0002. Send one self-addressed adhesive label to assist that office in processing your requests. See the SUPPLEMENTARY INFORMATION section for electronic access to the draft guidance document.

FOR FURTHER INFORMATION CONTACT: Lee Pai-Scherf, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, Rm. 2314, Silver Spring, MD 20993-0002, 301-796-3400; or Stephen Ripley, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 7301, Silver Spring, MD 20993-0002, 240-402-7911.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry entitled “Master Protocols: Efficient Clinical Trial Design Strategies to Expedite Development of Oncology Drugs and Biologics.” This guidance provides advice to sponsors of drugs and biologics for treatment of cancer regarding the design and conduct of clinical trials, other than FIH trials, intended to simultaneously evaluate more than one investigational drug and/or more than one cancer type within the same overall trial structure (master protocols) in adult and pediatric cancers.

There is increased interest in expediting late-stage drug development through developing trial designs that test multiple drugs and/or multiple cancer subpopulations in parallel under a single protocol, without a need to develop new protocols for every trial. The term *master protocol* is often used to describe the design of such trials, with variable terms such as *umbrella*, *basket*, or *platform* describing specific designs. Examples of trials using master protocols include the Lung-MAP trial (NCT02154490), the NCI-MATCH trial (EAY131, NCT02465060), and the Pediatric MATCH trial (APEC1621, NCT03155620). In contrast to traditional trial designs, where a single drug is tested in a single disease population in one clinical trial, master protocols use a single infrastructure, trial design, and protocol to simultaneously evaluate multiple drugs and/or disease populations in multiple substudies, allowing for efficient and accelerated drug development.

Because of the complexity of these trials evaluating multiple drugs and/or disease populations and the potential regulatory impact, it is important that such trials be well designed and well conducted to ensure patient safety and to obtain quality data that may support drug approval.

This draft guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the current thinking of FDA on "Master Protocols: Efficient Clinical Trial Design Strategies to Expedite Development of Oncology Drugs and Biologics." It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. This guidance is not subject to Executive Order 12866.

II. Paperwork Reduction Act of 1995

This draft guidance refers to previously approved collections of information found in FDA regulations. These collections of information are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act (PRA) of 1995 (44 U.S.C. 3501-3520).

FDA has OMB approval under the PRA (control number 0910-0014) for the submission of investigational new drug applications (INDs), including protocols, protocol amendments, and information amendments, in 21 CFR part 312, subpart B. Sponsors may request comment and advice on an IND as well as request meetings with FDA under 21 CFR part 312, subpart C (OMB control number 0910-0014). Responsibilities of sponsors and investigators (21 CFR part 312, subpart D) is also covered under OMB control number 0910-0014.

In addition, the following collections of information that have been approved by OMB would cover other submissions discussed in the draft guidance:

- Collections of information referred to in the guidance for industry entitled "Special Protocol Assessment" (available at <https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs->

gen/documents/document/ucm498793.pdf) have been approved under OMB control number 0910-0470;

- Collections of information referred to in the guidance for industry entitled “Establishment and Operation of Clinical Trial Data Monitoring Committees” (available at <https://www.fda.gov/downloads/regulatoryinformation/guidances/ucm127073.pdf>) have been approved under OMB control number 0910-0581;
- Collections of information referred to in the guidance for industry entitled “Oversight of Clinical Investigations — A Risk-Based Approach to Monitoring (available at <https://www.fda.gov/downloads/Drugs/Guidances/UCM269919.pdf>) has been approved under OMB control number 0910-0733;
- Collections of information referred to in the ICH guidance for industry entitled “E6(R2) Good Clinical Practice: Integrated Addendum to E6(R1) (available at <https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm464506.pdf>) has been approved under OMB control number 0910-0843.
- Collections of information in 21 CFR parts 50 and 56 have been approved under OMB control number 0910-0755;
- Collections of information under 21 CFR 56.115 have been approved under OMB control number 0910-0130;
- Collections of information referred to in the guidance for industry entitled “Expedited Programs for Serious Conditions--Drugs and Biologics,” (available at <https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm358301.pdf>) including fast track designation, breakthrough therapy designation, accelerated approval, and priority review designation, have been approved under OMB control number 0910-0765.
- Collections of information referred to in the draft guidance for industry entitled “Formal Meetings Between the FDA and Sponsors and Applicants for PDUFA Products” (available at <https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs->

gen/documents/document/ucm590547.pdf) have been approved under OMB control number 0910-0429;

- Requirements on content and format of labeling for human prescription drug and biological products have been approved under OMB control number 0910-0572.
- The submission of new drug applications, including 21 CFR 314.50(d)(5) (clinical data section) and (d)(6) (statistical section), has been approved under OMB control number 0910-0001.

In accordance with the PRA, before publication of any final guidance document, FDA intends to solicit public comment and obtain OMB approval for any information collections recommended in this guidance that are new or that would represent material modifications to those previously approved collections of information found in FDA regulations or guidances.

III. Electronic Access

Persons with access to the internet may obtain the draft guidance at either <https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>, <https://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>, or <https://www.regulations.gov>.

Dated: September 25, 2018.

Leslie Kux,

Associate Commissioner for Policy.

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